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Dose response curve fitting

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Updated date: Oct 21, 2020

An abbreviated version of this protocol was published in eLIFE in May 2015

The kinase DYRK1A reciprocally regulates the differentiation of Th17 and regulatory T cells

DOI: 10.7554/eLife.05920

Detailed protocol

Dose response curves for fractional enhancement of T_{reg} cell differentiation and culture cellularity were analyzed in Matlab to identify EC_{50} and LD_{50} doses, at which 50% T_{reg} enhancement and cytotoxicity are observed, respectively. Each compound was profiled across eight doses selected to sufficiently cover response dynamics. Dose response curves were fitted with either a single sigmoid or a double sigmoid function, depending on whether the response was asymptotic or impulse-like. An impulse function has the form:

$$f = \frac{1}{r_1} s(d : d_1, r_l, r_p, \alpha_1) \times s(d : d_2, r_h, r_p, \alpha_2),$$

where

$$s(d : d_m, r_i, r_f, \alpha) = r_i + (r_f - r_i) \frac{1}{1+e^{-4\alpha(d-d_m)}},$$

is a sigmoid function with a response that ranges from r_i to r_f with mid-point at dose d_m and a slope of $\alpha * \text{sign}(r_f - r_i)$ at dose d_m. The parameters of this model describe the dose of response onset (d_1), dose of response offset (d_2), initial response at lowest dose (r_l), peak response (r_p), final response at highest dose (r_h), and two slope parameters to model the rate of response onset (α_1) and offset (α_2). A single-sigmoid function uses only four parameters (d, r1, r2, α). All models were fitted to data using *fmincon* function in Matlab. Fitted models were reverse-queried to estimate the dose at which 50% of the peak response parameter was observed.

How to cite:（Readers should cite both the Bio-protocol preprint and the original research article where this protocol was used）

1. Xavier, R. (2020). Dose response curve fitting. Bio-protocol Preprint. bio-protocol.org/prep564.
2. Khor, B., Gagnon, J. D., Goel, G., Roche, M. I., Conway, K. L., Tran, K., Aldrich, L. N., Sundberg, T. B., Paterson, A. M., Mordecai, S., Dombkowski, D., Schirmer, M., Tan, P. H., Bhan, A. K., Roychoudhuri, R., Restifo, N. P., O'Shea, J. J., Medoff, B. D., Shamji, A. F., Schreiber, S. L., Sharpe, A. H., Shaw, S. Y. and Xavier, R. J.(2015). The kinase DYRK1A reciprocally regulates the differentiation of Th17 and regulatory T cells. eLIFE. DOI: 10.7554/eLife.05920

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